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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,601	02/19/2002	Olga Bandman	PF-0544USN	2590

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 11/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,601	BANDMAN ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-29,31-35,39 and 40* is/are pending in the application.

4a) Of the above claim(s) *32-35,39 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-29 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Amendment

1. Applicant's amendment filed on 8/10/04 is acknowledged.

Status of Claims

2 Claims 1-24, 30 and 36-38 are canceled.

Claims 25-29, 31-35, 39 and 40 have been amended and are pending in this application.

Claims 25-29 and 31 are under examination.

Claims 32-35, 39 and 40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

Priority

3. Upon Applicant's clarification (exhibit A filed on 8/10/04) on polynucleotide sequence of the SEQ.ID.NO: 11 in the present application is SEQ.ID.NO: 3 in priority Provisional Application **60/155,241,** 7/16/1998**,** the benefit of the filing date of provisional application has been accorded for the instant claims.

Claim Objections withdrawn

4. In view of the amendment to claims 23, 24,28 the objection is withdrawn.

Rejection(s) under 35 U.S.C § 112, Second Paragraph withdrawn

5. In view of the amendment to claims 25-29 and 31, the rejection under 35 U.S.C § 112, second paragraph is withdrawn.

Claim Rejection - 35 USC 102 (a) withdrawn

6. In view of the priority accorded as of 7/16/1998, the rejection of claims 25-29 and 31 under 35 U.S.C. 102(a) as being clearly anticipated by Cho et al Accession number AF126799 or J.B.C. 1999, 274, 471-477 is withdrawn.

Claim objections

7. Claims 25 and 26 are objected as they depend from higher numbered claim 31. Similarly claims 27, 28, 29 are also objected as improper dependent claims. Correction is required.

Claim Rejections - 35 USC § 101 maintained

8. The rejection of claims 25-29 and 31 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well-established utility is maintained as set forth in the previous office action.

When determining whether an applicant has described the utility of invention, one has to determine whether the applicant has described a well-established utility. If not, has the application made any assertion of utility and whether the asserted utility is a specific and credible utility.

In the instant case, the applicant claims a polynucleotide that has SEQ.ID.NO: 11and polynucleotide variant (90% identity). When the claims are interpreted in the light of the specification, the specification discloses that the invention relates to human oxidoreductase proteins (HORP 1-6) and polynucleotides that encode said polypeptides. The specification on page16 discloses that the claimed cytochrome b5 /desaturase HORP-5 shares 23% identity with sunflower cytochrome b5 /desaturase fusion protein. The specification does not provide any disclosure as to how the polypeptide encoded by the claimed polynucleotide is related to any and all of the regulatory molecules. Even if homology of some kind is (23% identity) present, the issue becomes that just because the claimed sequence would have homology to a certain known polypeptide, would it also have the function of the known polypeptide. The specification does not disclose as to how similar or different the functions of the claimed polynucleotide encoded polypeptide would have been from that of the list of polypeptides disclosed in the specification. If the function of the polypeptide is not established, how can its utility be established or be specific?

In light of the issue of function of the claimed polynucleotides, question also arises what will be the utility of the claimed polynucleotide? Logically, one would ask if an artisan did not know the function of a polynucleotide sequence, how would the artisan have known the consequence of the expression or inhibition of expression of such a polynucleotide sequence. Additionally, how would an artisan treat a disease for which the etiology or symptoms are not known or it is not known what disease would have

been caused by the polynucleotide or its encoded polypeptide. Likewise how would an artisan have screened for compounds that affect the function of a polypeptide if the artisan had not known the function of the polypeptide. Furthermore, if the function of a protein is not established, what would have been the use and basis for developing an assay system?
Claims 23-29 and 31 in the currently written form, would encompass the polynucleotide and variant thereof from all the living organisms. It is, therefore concluded that because the function of the SEQ. ID NO: 11 is not disclosed, the credibility of the asserted utilities for the claims 23-29 and 31 cannot be assessed.

In the event that the rejection less than 35 USC101 might be overcome, the following grounds of rejection would still apply. Claims 23-29 and 31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. The written description rejection of claims 25-29 and 31 under 35 U.5.C. 112, first paragraph, is maintained

The specification only describes a polynucleotide sequence of SEQ ID NO: 11. The specification describes as part of the invention-isolated polynucleotide encoding the polypeptide of SEQ ID NO: 5, which is described as Human oxidoreductase polypeptide HORP 5. However, broadly claimed nucleic acid sequence which is at least 90% identical to said nucleic acid (The examiner consider the sequence as variant and will be addressed as variants in the Office action) are not set forth in this specification. Applicants also broadly describe the invention as embracing any substitution, insertion or deletion change of nucleotides throughout the entire stretch of nucleotides by use of language in which a specified percent of amino acids can be changed. As depending from these are the vector, host cell, vaccine, diagnostics and methods of producing the polypeptide. None of these sequences meets the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116)
The specification only discloses a polynucleotide sequence consisting of SEQ ID NO: 11 which corresponds to the polynucleic acid sequence encoding the polypeptide SEQ ID N0: 5. However, the function of the polynucleotide and variant are not known.

The claimed polynucleotide variant that encodes such protein can only be determined empirically by actually making every nucleic acid that encodes the recited variability (i.e. the instant variant) and testing each to determine whether it encodes a protein having the particularly disclosed properties. As noted in the Guidelines at Section I.A (2). There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonable predict the complete structure of the claimed invention from its function. There is no written description support for claimed polynucleotide or its variant as claimed.

The protein has specific biological properties dictated by the structure of the protein and the corresponding structure of the structural gene sequence which encodes it. There must be some nexus between the structure of a polynucleotide sequence, the protein encoded, and the **function** of that encoded protein. The specification fails to teach the function of the claimed polynucleotide or its variant, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016.

10. The enablement rejection of claims 25-29 and 31 under 35 U.S.C. 112, first paragraph, is maintained as set forth in the previous office action.

To decide whether a specification is enabling, it is to be determined whether the specification discloses sufficient guidelines for successful making and using of the claimed invention without undue experimentation and whether sufficient examples have been provided. As described above (in written description rejection), the specification fails to describe sufficient guidelines for a skilled artisan to have practiced the invention as claimed without undue experimentation because the specification does not provide sufficient guidance for using the invention.

Applicants' arguments filed on 8/10/04, have been fully considered but they are not deemed to be persuasive.

With respect to 35 U.S.C.101 and 112, first paragraph rejections,

(A) Applicant states that the specification sufficiently describes the invention to a known sunflower protein cytochrome b5/desaturase fusion protein and the specification provides sufficient disclosure of the relationship of the inventive polypeptide to known oxidoreductase proteins, such as cytochrome b5/desaturase fusion protein. The specification explicitly describes the polynucleotide sequence having structure as shown by SEQ.ID.NO: 11, having 23% identity to sunflower cytochrome b5/desaturase fusion protein including heme binding site, transmembrane domains etc. Additional description in the specification regarding the relationship of inventive polypeptides to known protein is provided, for example, in Table 2 at page 60. Tabl 2 lists signature

sequences such as sequences pertaining to transmembrane domains, heme-binding domains, and cytochrome b5 signature sequences as shown in SEQ.ID.NO: 5.

(B) Applicant states that the specification describes biological properties of polynucleotide such as tissue expression and particularly RNA expression of invention polynucleotide in various types of tissue libraries. For instance, the specification states: northern analysis shows the expression of SEQ D NO: 11 in various libraries at least 59% of which are immortalized or cancerous, at least 26% of which involve immune response, and at least 23% of which are fetal or proliferating cell or tissues. Of particular role is the expression of SEQ. ID.NO: NO 11 in male and female reproductive, nervous, cardiovascular and endocrine tissue.

The examiner disagrees with the applicant (A: structure and B: biological activity) because the variants/fragments as claimed previously are rightly rejected under Utility and written decryption and the examiner indicated that such variants/fragments do not set forth structure and properties etc. However, as amended now the specification discloses an isolated polynucleotide and encoding protein in SEQ.ID.NO: 11 and 5 respectively and is not supported by either a specific utility or a well established utility. The specification fails to provide support for polynucleotide sequence having 90% identity. Claims are drawn to a polynucleotide comprising a polynucleotide sequence, SEQ.ID.NO: 11 or 90%identity to said sequence. The specification on page16 discloses that the claimed cytochrome b5 /desaturase HORP-5 shares 23% identity with sunflower cytochrome b5 /desaturase fusion protein. Based on the structural similarity, the specification asserts that the newly disclosed HORP has the utility of having similar activities. The disclosed HORP have biological activities similar to known sunflower cytochrome b5/desaturase fusion protein, is not credible in the absence of supporting evidence, because the relevant literature reports (please note, the examiner is citing all

the references as supporting evidence for applicant's arguments) numerous examples of polypeptide families having similarities but individual members have distinct, and even opposite, biological activities. For example, Hitomi et al (US Patent 6,313,267) states that calcium-binding proteins with EF-hands are diverse in function (see column 1, lines 18-37). In addition, Tischer et al. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences between PDGF and VEGF are also seen in vivo, wherein endothelial-pericyte associations in the eye are disrupted by intraocular administration of PDGF but accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598., see Abstract and pp. 1594-1596). Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF-β family members BMP-2 and TGF-β I had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). See also Massague, who reviews other members pf the TGF-β family (1987, Cell 49:437-8, sp. p. 438, column 1, second full paragraph to the end).

Similarly, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone 14:717-720., see p. 717, second paragraph of Introduction). Finally, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48).

With respect to written description rejection, Applicant states (A) The Specification sufficiently describes the claimed invention and (B) Specification sufficiently describes inventive Polypeptides. Further, applicant states that the application describes the structure of the polynucleotide as SEQ.ID.NO: 11 and is related to sunflower cytochrome b5 /desaturase fusion protein and polynucleotide having % identity has been described by using Mcalign program™.

The examiner disagrees with the applicant because the claimed polynucleotide as shown in SEQ.ID.NO: 11 although related to sunflower cytochrome b5 /desaturase but the function of cytochrome b5 /desaturase is not described either in sunflower or in the present polynucleotide. Generally, the art acknowledges reports (please note, the examiner is citing all the references as supporting evidence for applicant's arguments) that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Bork et al (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Finally, Bowie et al. (1990, Science 247:1306-1310) state that determination of three dimensional structure from primary amino acid sequence, and the subsequent inference of detailed aspects of function from structure is extremely complex and unlikely to be solved in the near future (p. 1306). Thus, the specification fails to support the asserted credible, specific and substantial utility of HORP. The specification

does not support a credible, specific and substantial utility regarding the claimed polynucleotide thereof for purposes unrelated to the asserted biological activity of the polypeptide.

Applicant states that SEQ D NO: 11 has been shown to express in various libraries or fetal or proliferating cell or male and female reproductive or nervous or cardiovascular or endocrine tissue.

The examiner understands that the claimed polynucleotide is expressed in libraries, fetal, proliferating cell or male and female reproductive or nervous or cardiovascular or endocrine tissue. without a disclosure of a particular disease state in which the polypeptides are expressed at an altered level or form, it would be impossible to determine what the results of a gene expression monitoring assay mean. The asserted utility in gene expression monitoring assays is thus not substantial, because significant further research would have to be conducted to determine which diseases correlate with altered forms or levels of the polynucleotide and polypeptide, and whether the polynucleotide and polypeptides are over expressed or under expressed in the diseased tissue. The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a credible, specific and substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner v. Manson, 148 USPQ at 696.

Claim Rejection - 35 USC 102 maintained

11. The rejection of claims 25-29 and 31 under 35 U.S.C. 102(e) as being anticipated by Mukerji et al U.S.Patent 6,428,990 or 6,432,684 is maintained as set forth in the previous office action.

Mukerji et al disclose an isolated polynucleotide comprising a polynucleotide sequence (a polynucleotide reads on less than SEQ.ID.NO: 11) SEQ.ID.NO: 8, vector, a host cell transformed with said polynucleotide and method of producing polypeptide (see example 1,2 and 3). Thus the disclosed polynucleotide anticipated the instantly (see the enclosed sequence alignment) claimed invention.

Please note the 102 (e) date for U.S.Patent 6,428,990 or 6,432,684 is 4/11/1997 and not the filing date of the application as applicant asserts. Therefore, the rejection is maintained.

Remarks

12. No claims are allowed.

Conclusion

13. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

14. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which

receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

15. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

16. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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